Oxlumo (Lumasiran) for Primary Hyperoxaluria Type 1 (PH1)

- overproduction, leading to kidney stones and organ damage.
- Oxlumo (Alnylam) is an RNAi drug that inhibits HAO1 gene to reduce oxalate production.
- Approved by FDA (US), EMA (EU), and Health Canada for adults and children (≥4 months).
- Clinical trials (ILLUMINATE-A/B) show ~65–72% reduction in urinary oxalate.
- Benefits include improved kidney outcomes and quality of life; well-tolerated with mild injection site reactions.
- Reimbursed in Canada (CADTH), UK (NICE/NHS), and covered by U.S. insurers with Alnylam support.
- Access criteria: confirmed PH1, elevated oxalate, specialist prescription. Discontinue if no response.

Brineura for CLN2 Disease

- **What is CLN2 (form of Batten disease):** A deficiency of an enzyme (TPP1) causing neurodegeneration, seizures, and early death.
- **How does Brineura work to treat CLN2**: Replaces the TPP1 enzyme; administered directly into the brain (CSF) every two weeks.
- **What patients are approved for treatment by regulators (FDA, EMA, Canada):** Approved for pediatric patients with confirmed CLN2—initially age 3+, now expanded to all ages.
- **What are the benefits**: Slows the decline in motor and language function; improves quality of life.
- **What are (general) criteria for access and criteria for discontinuation:** Confirmed diagnosis; baseline motor-language score ≥3; discontinue if significant function loss.
- **When were these criteria defined and have they been updated based on real-world data:** Defined 2017–2018; generally unchanged, but monitored via managed access programs.
- **What are consequences of discontinuation in terms of disease progression**: Progression typically resumes quickly; patients lose motor/language function and die young.

Cablivi (caplacizumab) for aTTP: Summary Overview

- aTTP is a rare, life-threatening autoimmune disorder due to ADAMTS13 deficiency.
- Cablivi is a nanobody therapy targeting vWF, approved for adult aTTP in EU, US, Canada.
- Administered with plasma exchange and immunosuppressants.
- Benefits: Faster platelet normalization, fewer relapses, reduced death/thrombotic events.
- Side effects: Common—nosebleeds, headaches; Rare—severe/fatal bleeding.
- CADTH (Canada) did not recommend reimbursement due to high cost and limited long-term benefit data.
- Some private insurers may cover but no supply in Canada now; reimbursement available in NHS Scotland and select EU countries.

Sohonos (palovarotene) for FOP – Summary

- FOP (Fibrodysplasia Ossificans Progressiva) is a rare genetic disease causing abnormal bone growth in soft tissue.
- Sohonos (palovarotene) is a selective RARγ agonist that reduces heterotopic ossification by inhibiting chondrogenesis.
- Approved in: USA (FDA, Aug 2023), Canada (Jan 2022), UAE (conditional). Not approved in the EU.
- Indicated for adults and children (females ≥8, males ≥10 years).
- Clinical impact: Significant reduction in new HO (0.4 vs. 20.3 cm^3/year), preserves mobility, fewer flare-ups.
- Common side effects: dry skin, joint pain, fatigue, growth plate closure risk in children.
- Reimbursed in Canada (CADTH recommendation); US access via Ipsen Cares program.
- Requires specialist monitoring; contraindicated during pregnancy.

Evkeeza (evinacumab) for HoFH – Summary

- HoFH: Rare genetic disorder (~1 in 250,000–400,000) causing severe LDL-C elevation due to defective LDL receptors.
- Evkeeza: Monoclonal antibody inhibiting ANGPTL3; reduces LDL-C independent of LDL receptors.
- Approvals: FDA (≥5 yrs), EMA (≥6 months), reimbursed in US, Canada, EU (several countries), Japan.
- Benefits: ~48% LDL-C reduction in 24 weeks; lowers cardiovascular risk; improves QoL.
- Adverse Effects: Nasopharyngitis, flu-like symptoms, dizziness, rare hypersensitivity.
- Access: Add-on for HoFH with high LDL-C despite other therapies; review after 24 weeks.
- Alternatives: Apheresis (invasive), Lomitapide (GI/liver issues), Liver transplant (rare, high risk).

Voxzogo for Infants with Achondroplasia (<12 Months)

Voxzogo (vosoritide) is approved for infants in select countries (e.g., USA, Japan).

- It targets the FGFR3 pathway to promote bone growth.

Potential Benefits for Infants:

- Greater height potential by treating during rapid early growth.
- May reduce serious complications (e.g., brainstem compression, hydrocephalus).
- Potential for improved motor milestone achievement (e.g., sitting, crawling).
- Psychosocial benefits for families from early intervention.

Ongoing Studies:

- Clinical trials are assessing safety, growth, neurological development, and quality of life.
- Long-term impact and optimal dosing are still being studied.